510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

K043327

B. Purpose for Submission:

New submission

C. Measurand:

Benzodiazepine

D. Type of Test:

Qualitative/Semi-Quantitative/ Immunoassay

E. Applicant:

Roche Diagnostics

F. Proprietary and Established Names:

ONLINE DAT Benzodiazepines Plus

G. Regulatory Information:

1. Regulation section:

   21 CFR section 862.3170 - Enzyme Immunoassay, Benzodiazepine

2. Classification: Class II

3. Product code: JXM

4. Panel: 91 (Toxicology)

H. Intended Use:

1. Intended use(s):

The ONLINE DAT Benzodiazepines Plus is an in vitro diagnostic test for the qualitative and semi-quantitative detection of benzodiazepines in human urine on automated clinical chemistry analyzers at cutoff concentrations of 100 ng/mL, 200 ng/mL, and 300 ng/mL. Semi-quantitative test results may be obtained that permit laboratories to assess assay performance as part of a quality control program.

Benzodiazepines: 100 Cutoff: 2.1 ng/mL nordiazepam
200 Cutoff: 3.8 ng/mL nordiazepam
300 Cutoff 7.6 ng/mL nordiazepam

2. Indication(s) for use:

The ONLINE DAT Benzodiazepines Plus is an in vitro diagnostic test for the qualitative and semi-quantitative detection of benzodiazepines in human urine on automated clinical chemistry analyzers at cutoff concentrations of 100 ng/mL, 200 ng/mL, and 300 ng/mL. Semi-quantitative test results may be obtained that permit laboratories to assess assay performance as part of a quality control program.

3. Special conditions for use statement(s):

The ONLINE DAT Benzodiazepines Plus Assay provides only a preliminary analytical test result. A more specific alternative chemical method must be used to obtain a confirmed analytical result. Gas chromatography/Mass spectrometry is the preferred confirmatory method. Other chemical confirmation methods are available. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

The assay is for Prescription Use.

Semi-quantitative results may be helpful in estimating the concentrations of drug(s) in samples. This can aid users when they are preparing dilutions of the samples for further analysis.

4. Special instrument requirements:

Performance was demonstrated in this submission on the Roche Hitachi 917 analyzer. In addition to the Hitachi 917 reagent application included in this

filing, Roche Diagnostics plans to apply the ONLINE DAT Benzodiazepines Plus reagent to the following Hitachi analyzers:

* Hitachi 911 – A II level application
* Hitachi 912 – A I level application
* Modular P - A II level application
* Modular DAT – A I level application

Reagent performance validations have been performed with the ONLINE DAT Benzodiazepines Plus reagent in accordance with Roche Diagnostics minimum requirements application validation protocol. Master application level work as described in this submission was completed on the Hitachi 917 analyzer for the Benzodiazepines Plus assay, following FDA's Replacement Reagent and Instrument Family Policy guidance and Roches internal application protocol. The Benzodiazepines Plus assay was validated on other members of the Hitachi family with successful completion of A I or A II level application works.

I. Device Description:

The device consists of two wet reagents which contain the key components of the immunoassay; monoclonal/ polyclonal antibody against the drug, substrate, and enzyme-labeled drug (conjugate).

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Roche Abuscreen OnLine Benzodiazepines Assay

2. Predicate 510(k) number(s):

   k983702

3. Comparison with predicate:

The following table illustrates the similarities and differences between the Roche ONLINE DAT Benzodiazepines Plus assay and the predicate device.

Feature	Roche Abuscreen OnLine Benzodiazepines (Predicate)	Roche ONLINE DAT Benzodiazepines Plus
Methodology	KIMS, Kinetic interaction of microparticles in a solution	KIMS, Kinetic interaction of microparticles in a solution
Reagents	Antibody Working Solution: Benzodiazepines polyclonal antibody (sheep) in buffer with bovine serum albumin, and	Antibody Working Solution: Benzodiazepines polyclonal antibody (sheep) in buffer with bovine serum albumin, and 0.09% sodium azide

Feature	Roche Abuscreen OnLine Benzodiazepines (Predicate)	Roche ONLINE DAT Benzodiazepines Plus
	preservative. Microparticle Working Solution: Microparticles coated with conjugated benzodiazepine derivatives in a buffer and preservative.	 Microparticle Working Solution: Microparticles coated with conjugated benzodiazepine derivatives in a buffer and 0.09% sodium azide.
Sample Type	Urine	Urine
Controls	Abuscreen OnLine Positive Control and Negative Control, and Abuscreen OnLine Benzodiazepine Special Controls	Control Sets DAT I, DAT II and DAT III
Calibrators	Abuscreen OnLine Preciset DAT I and DAT II and Abuscreen OnLine Cfas DAT Qualitative calibrator sets.	Preciset DAT Plus I and Plus II, Cfas DAT Qualitative Plus and Cfas DAT Qualitative Clinical calibrator set.
Calibrator Levels ng//mL	100 ng/mL Qualitative (1 point calibration): Abuscreen OnLine Preciset DAT I, Cal 3 or Cfas DAT Qualitative: 100 ng/mL 100 ng/mL Semiqualitative: A.O. Preciset DAT I, Cal 1,0 ng/mL A.O. Preciset DAT I, Cal 2, 50 ng/mL A.O. Preciset DAT I, Cal 3, 100 ng/mL A.O. Preciset DAT I, Cal 4, 200 ng/mL 200 ng/mL Qualitative (1 point calibration): Abuscreen OnLine Preciset DAT I, Cal 4: 200 ng/mL 200 ng/mL Semiquantitative: A.O. Preciset DAT I, Cal 1,0 ng/mL A.O. Preciset DAT I, Cal 3, 100 ng/mL A.O. Preciset DAT I, Cal 4, 200 ng/mL A.O. Preciset DAT I, Cal 7, 400 ng/mL 300 ng/mL Qualitative: (1 point calibration): Abuscreen OnLine Preciset DAT II, Cal 5: 300 ng/mL 300 ng/mL Semiquantitative: A.O. Preciset DAT I, Cal 1,0 ng/mL A.O. Preciset DAT I, Cal 6, 150 ng/mL A.O. Preciset DAT I, Cal 5, 300 ng/mL A.O. Preciset DAT I, Cal 8, 600 ng/mL	100 ng/mL Qualitative (1 point calibration): Preciset DAT II, Cal 3, or Cfas DAT Qualitative Clinical, Cal 2: 100 ng/mL 100 ng/mL Semiquantitative: Preciset DAT Plus II, Cal 1, 0 ng/mL Preciset DAT Plus II, Cal 2, 50 ng/mL Preciset DAT Plus II, Cal 3, 100 ng/mL Preciset DAT Plus II, Cal 4, 200 ng/mL 200 ng/mL Qualitative: (1 point calibration): Preciset DAT Plus II, Cal 4: 200 ng/mL 200 ng/mL Semiquantitative: Preciset DAT Plus II, Cal 1, 0 ng/mL Preciset DAT Plus II, Cal 3, 100 ng/mL Preciset DAT Plus II, Cal 4, 200 ng/mL Preciset DAT Plus II, Cal 5, 400 ng/mL 300 ng/mL Qualitative: (1 point calibration): Preciset DAT Plus I, Cal 3, or Cfas DAT Qualitative Plus, or Cfas DAT Qualitative Clinical, Cal 1: 300 ng/mL 300ng/mL Semiquantitative: Preciset DAT Plus II, Cal 1, 0 ng/mL Preciset DAT Plus II, Cal 2, 150 ng/mL Preciset DAT Plus II, Cal 3, 300 ng/mL Preciset DAT Plus II, Cal 4, 600 ng/mL
Sensitivity	100 Cutoff: 17 ng/mL nordiazepam	100 Cutoff: 2.1 ng/mL nordiazepam

Feature	Roche Abuscreen OnLine Benzodiazepines (Predicate)	Roche ONLINE DAT Benzodiazepines Plus
(LOD) Limit of Detection	200 Cutoff: 40 ng/mL nordiazepam 300 Cutoff: 36 ng/mL nordiazepam	200 Cutoff: 3.8 ng/mL nordiazepam 300 Cutoff: 7.6 ng/mL nordiazepam
Method comparison, 100 ng/mL Cutoff	OnLine Benzodiazepines / GC/MS + 50 / 50 - 0 / 0	Benzodiazepines Plus / GC/MS + 82 / 82 - 10 / 10
Method Comparison, 200 ng/mL Cutoff	OnLine Benzodiazepines / GC/MS + 50 / 50 - 0 / 0	Benzodiazepines Plus / GC/MS + 76 / 78 - 12 / 10
Method Comparison, 300 ng/mL Cutoff	OnLine Benzodiazepines / GC/MS + 50 / 50 - 0 / 0	Benzodiazepines Plus / GC/MS + 72 / 72 - 10 / 10
SQ Precision	100 ng/mL	100 ng/mL
Within Run Target: Mean (ng/mL) CV%	50 / 75 / 100 / 125 / 150 / 200 51 / 75 / 102 / 130 / 148 / 202 4.4 / 2.8 / 2.3 / 2.0 / 2.0 / 1.4	50 / 75 / 100 / 125 / 150 47.5 / 75.2 / 99.9 / 130.7 / 157.8 2.1 / 1.3 / 1.5 / 0.7 / 0.7
Day to day Target: Mean (ng/mL) CV%	50 / 75 / 100 / 125 / 150 / 200 52 / 76 / 101 / 128 / 152 / 202 6.0 / 3.5 / 3.2 / 3.6 / 2.7 / 1.8	50 / 75 / 100 / 125 / 150 47.3 / 76.9 / 100.9 / 131.6 / 158.6 2.7 / 1.7 / 1.7 / 1.1 / 1.1
SQ Precision	200 ng/mL	200 ng/mL
Within Run Target: Mean (ng/mL) CV%	100 / 150 / 200 / 250 / 300 96 / 141 / 200 / 251 / 315 4.4 / 2.7 / 1.9 / 1.5 / 1.2	100 / 150 / 200 / 250 / 300 97.7 / 154.4 / 197.2 / 258.2 / 314.4 2.1 / 1.0 / 1.2 / 0.7 / 0.8
Day to day Target: Mean (ng/mL) CV%	100 / 150 / 200 / 250 / 300 100 / 145 / 205 / 258 / 320 5.3 / 3.3 / 2.1 / 2.2 / 2.0	100 / 150 / 200 / 250 / 300 98.8 / 155.3 / 197.3 / 259.1 / 313.8 2.7 / 1.2 / 1.6 / 0.8 / 0.9
SQ Precision	300 ng/mL	300 ng/mL
Within Run Target: Mean (ng/mL) CV%	150 / 225 / 300 / 375 / 450 152 / 224 / 301 / 388 / 465 2.1 / 1.2 / 1.4 / 1.1 / 0.7	150 / 225 / 300 / 375 / 450 154.5 / 227.7 / 305.4 / 384 / 434.8 1.3 / 1.0 / 1.0 / 0.8 / 0.8
Day to day Target: Mean (ng/mL) CV%	150 / 225 / 300 / 375 / 450 154 / 228 / 306 / 394 / 470 2.7 / 1.8 / 2.0 / 1.7 / 4.3	150 / 225 / 300 / 375 / 450 153.1 / 223.8 / 301.2 / 377.3 / 438.3 1.8 / 1.5 / 1.4 / 1.2 / 1.9
Indications for use	The Roche Abuscreen OnLine assay for Benzodiazepines is an in vitro diagnostic test for the qualitative and semi-quantitative detection of benzodiazepines in human urine on automated clinical chemistry analyzers at cutoff concentrations of 100 ng/mL, 200 ng/mL and 300	Benzodiazepines Plus is an in vitro diagnostic test for the qualitative and semi-quantitative detection of benzodiazepines in human urine on automated clinical chemistry analyzers at cutoff concentrations of 100 ng/mL, 200 ng/mL and 300 ng/mL. Semi-quantitative test results may be obtained that permit

Feature	Roche Abuscreen OnLine Benzodiazepines (Predicate)	Roche ONLINE DAT Benzodiazepines Plus
Indications for use (cont.)	ng/mL. Semi-quantitative test results may be obtained that permit laboratories to assess assay performance as part of a quality control program.	laboratories to assess assay performance as part of a quality control program.
Qualitative and Semi-Quantitative cutoffs	100, 200, and 300 ng/mL	100, 200, and 300 ng/mL

K. Standard/Guidance Document Referenced (if applicable):

FDA's Replacement Reagent and Instrument Family Policy Guidance.

L. Test Principle:

The test is an enzyme immunoassay for use on automated clinical chemistry analyzers. Calibrators, ranging in concentration from 0 to 600 ng/mL, are run with the assay. Enzyme-labeled drug and drug present in the sample compete for limited antibody binding sites. Binding of the enzyme-labeled drug inhibits its reaction with the substrate, thereby influencing the rate of absorbance change measured by the instrument. The rate of absorbance change is proportional to the concentration of drug in the sample. Concentrations of controls and unknowns are calculated from the standard curve.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

(All performance was established on the Roche Hitachi 917 analyzer unless otherwise noted.)

The imprecision of the ONLINE DAT Benzodiazepines Plus assay at the 100, 200 and 300 ng/mL cutoffs was determined by running a series of calibrators and controls in replicates of 20 per day for five days on a Hitachi 917 analyzer. The following results were obtained:

Acceptance criteria: 100 ng/mL Cutoff

Within-run imprecision ≤ 8% CV
(≤ 10% CV for 50 & 150 ng/mL)
Run-to-run Imprecision ≤ 10% CV
(≤ 12% CV for 50 & 150 ng/mL)
Near cutoff Imprecision ≤ 5% Crossovers

Within-run Imprecision (N = 20), 100 ng/mL cutoff

	Semi-quantitative		Qualitative	
Cals)/ Controls (ng/mL)	Mean (ng/mL)	CV%	Mean (mAbs)	CV%
.50 X (50)	47.5	2.1%	575.4	0.6%
.75 X (75)	75.2	1.3%	473.8	0.6%
Cutoff (100)	99.9	1.5%	400.2	1.0%
1.25 X (125)	130.7	0.7%	312.8	1.0%
1.50 X (150)	157.8	0.7%	249.1	1.1%

Day-to-day Imprecision (N = 100), 100 ng/mL cutoff

	Semi-quantitative		Qualitative	
Cals)/ Controls (ng/mL)	Mean (ng/mL)	CV%	Mean (mAbs)	CV%
.50 X (50)	47.3	2.7%	580.8	0.8%
.75 X (75)	76.9	1.7%	473.9	0.7%
Cutoff (100)	100.9	1.7%	400.8	1.0%
1.25 X (125)	131.6	1.1%	312.7	1.0%
1.50 X (150)	158.6	1.1%	246.8	1.2%

Near cutoff Imprecision, 100 ng/mL

Controls (ng/mL)	Number Tested	Correct Results	Confidence Level
.75 X (75)	100	100	> 95% negative reading
1.25 X (125)	100	100	> 95% positive reading

Acceptance criteria: 200 ng/mL Cutoff

Within-run imprecision ≤ 8% CV
(≤ 10% CV for 100 & 300 ng/mL)
Run-to-run Imprecision ≤ 10% CV
(≤ 12% CV for 50 & 150 ng/mL)
Near cutoff Imprecision ≤ 5% Crossovers

Within-run Imprecision (N = 20), 200 ng/mL cutoff

	Semi-quantitative		Qualitative	
Cals)/ Controls (ng/mL)	Mean (ng/mL)	CV%	Mean (mAbs)	CV%
.50 X (100)	97.7	2.1%	624.0	0.7%
.75 X (150)	154.4	1.0%	501.2	0.8%
Cutoff (200)	197.2	1.2%	431.8	1.1%
1.25 X (250)	258.2	0.7%	323.2	0.9%
1.50 X (300)	314.4	0.8%	248.1	1.2%

Day-to-day Imprecision (N = 100), 200 ng/mL cutoff

	Semi-quantitative		Qualitative	
Cals)/ Controls (ng/mL)	Mean (ng/mL)	CV%	Mean (mAbs)	CV%
.50 X (100)	98.8	2.7%	623.4	0.7%
.75 X (150)	155.3	1.2%	501.4	0.7%
Cutoff (200)	197.3	1.6%	423.8	2.0%
1.25 X (250)	259.1	0.8%	320.7	1.4%
1.50 X (300)	313.8	0.9%	245.0	1.6%

Near cutoff Imprecision, 200 ng/mL

Controls (ng/mL)	Number Tested	Correct Results	Confidence Level
.75 X (150)	100	100	> 95% negative reading
1.25 X (250)	100	100	> 95% positive reading

Acceptance criteria: 300 ng/mL Cutoff

Within-run imprecision ≤ 8% CV
(≤ 10% CV for 150 & 450 ng/mL)
Run-to-run Imprecision ≤ 10% CV
(≤ 12% CV for 150 & 450 ng/mL)
Near cutoff Imprecision ≤ 5% Crossovers

Within-run Imprecision (N = 20), 300 ng/mL cutoff

	Semi-quantitative		Qualitative	
Cals)/ Controls (ng/mL)	Mean (ng/mL)	CV%	Mean (mAbs)	CV%
.50 X (150)	154.5	1.3%	599.0	0.8%
.75 X (225)	227.7	1.0%	475.6	0.7%
Cutoff (300)	305.4	1.0%	365.0	0.9%
1.25 X (375)	384.0	0.8%	276.3	0.9%
1.50 X (450)	434.8	0.8%	219.9	1.8%

Day-to-day Imprecision (N = 100), 300 ng/mL cutoff

	Semi-quantitative		Qualitative	
Cals)/ Controls (ng/mL)	Mean (ng/mL)	CV%	Mean (mAbs)	CV%
.50 X (150)	153.1	1.8%	598.1	1.0%
.75 X (225)	223.8	1.5%	474.7	1.0%
Cutoff (300)	301.2	1.4%	365.2	1.2%
1.25 X (375)	377.3	1.2%	274.5	1.4%
1.50 X (450)	438.3	1.9%	216.3	3.9%

Near cutoff Imprecision, 300 ng/mL

Controls (ng/mL)	Number Tested	Correct Results	Confidence Level
.75 X (225)	100	100	> 95% negative reading
1.25 X (375)	100	100	> 95% positive reading

b. Linearity/assay reportable range:

Not applicable. The assay is intended for qualitative use.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Unassayed multi-analyte controls used for these qualitative and semi-quantitative applications are Control Set DAT I, Control Set DAT II, and Control Set DAT III, targeted at 0.75x for the negative control and 1.25x for the positive control relative to each of the 100, 200, and 300, ng/mL assay cutoffs.

The multi-analyte calibrator sets used for the Benzodiazepines Plus application are Preciset DAT Plus I (K031775) and Preciset DAT Plus II (K033306). In addition, C.f.a.s. DAT Qualitative Plus (K033306), a single level, multi-analyte qualitative calibrator can also be used for the calibration of the qualitative assay at a 300 ng/mL cutoff. Finally, C.f.a.s. DAT Qualitative Clinical, a 5 level, multi-analyte calibrator set, can also be used for the benzodiazepines qualitative assay at 100 or 300 ng/mL cutoffs. This calibrator set is comprised completely of qualified bottles into a new kit configuration from 5 existing Roche DAT calibrator sets listed as follows: Preciset DAT Plus I, level 4 (K031775), Preciset DAT Plus II, level 3 and C.f.a.s. DAT Qualitative Plus (K033306), Preciset DAT THC, level 3 (K033246) and Preciset DAT Amphetamine, level 4 (K033265)

Calibrators and controls are required with this assay and are specifically identified in the labeling. They are both provided separately, and have been previously cleared.

STABILITY

Product shelf-life claims for the R1 reagent (bottle 1 diluent and bottle 1a antibody) and the R2 conjugated drug derivative/ microparticle reagent will be established based on real-time stability studies. At least one lot of the reagent will be tested up to or exceeding the product shelf life claim (expiration date) before commercializing the product.

Real time stability testing is conducted on product stored at 2° - 8° C over the claimed shelf life. Product is tested at time 0, and at approximately 50%, 75% and

100% of the shelf life claim. Testing includes ≤ 5% crossovers at the cutoff when tested at 0.75x and 1.25x relative to the 300 ng/mL cutoff. All protocols, acceptance criteria, and data will be kept on file at Roche Diagnostics.

d. Detection limit:

Sensitivity of the assay at cutoffs of 100, 200 and 300 ng/mL.

The limit of detection (or analytical sensitivity) of the ONLINE DAT Benzodiazepines Plus at a **100 ng/mL** cutoff was performed by testing 21 replicates of the 0 ng/mL standard. Two standard deviations above the mean yields a limit of detection of 2.1 ng/mL benzodiazepines.

Calculation		
	Std 1	Std 2
Conc	0	50
Mean	776.9	559.0
SD	4.8	
2 SD	9.2	
3 SD	13.8	
Slope	-0.2294	
Analytical Sensitivity		
@ 2 SD	2.1	
@ 3 SD	3.2	

The limit of detection (or analytical sensitivity) of the ONLINE DAT Benzodiazepines Plus at a **200 ng/mL** cutoff was performed by testing 21 replicates of the 0 ng/mL standard. Two standard deviations above the mean yields a limit of detection of 3.8 ng/mL benzodiazepines.

Calculation		
	Std 1	Std 2
Conc	0	100
Mean	860.4	610.1
SD	4.7	
2 SD	9.5	
3 SD	14.2	
Slope	-0.3995	
Analytical Sensitivity		
@ 2 SD	3.8	
@ 3 SD	5.7	

The limit of detection (or analytical sensitivity) of the ONLINE DAT Benzodiazepines Plus at a **300 ng/mL** cutoff was performed by testing 21 replicates of the 0 ng/mL standard. Two standard deviations above the mean yields a limit of detection of 7.6 ng/mL benzodiazepines.

Calculation		
	Std 1	Std 2
Conc	0	150
Mean	895.8	600.1
SD	7.5	
2 SD	15.0	
3 SD	22.5	
Slope	-0.5074	
Analytical Sensitivity		
@ 2 SD	7.6	
@ 3 SD	11.4	

e. Analytical specificity:

The specificity of Benzodiazepines Plus for various benzodiazepines and benzodiazepine metabolites was determined by generating inhibition curves for each of the compounds listed and determining the approximate quantity of each compound that is equivalent in assay reactivity to a 100, 200, and 300 ng/mL nordiazepam assay cutoff.

Benzodiazepines

Compound	Response equivalent to 100 ng/mL Nordiazepam	Approximate Percent Cross-reactivity
Alprazolam	108	93
Chlordiazepoxide	148	68
Diazepam	106	94
Oxazepam	122	82
Clonazepam	148	68
Flunitrazepam	142	71
Nitrazepam	114	88

Benzodiazepines

Compound	Response equivalent to 200 ng/mL Nordiazepam	Approximate Percent Cross-reactivity
Alprazolam	219	91
Chlordiazepoxide	318	63
Diazepam	215	93
Oxazepam	259	77
Clonazepam	307	65
Flunitrazepam	283	71
Nitrazepam	246	81

Benzodiazepines

Compound	Response equivalent to 300 ng/mL Nordiazepam	Approximate Percent Cross-reactivity
Alprazolam	338	89
Chlordiazepoxide	486	62
Diazepam	340	88
Oxazepam	398	75
Clonazepam	445	67
Flunitrazepam	424	71
Nitrazepam	359	84

f. Assay cut-off:

Assay cutoff 100, 200, and 300 ng/mL. (See precision/reproducibility section above.

2. Comparison studies:

a. Method comparison with predicate device:

Because the candidate device was compared to a reference method, GC/MS, it was not compared to a predicate device.

Accuracy – Clinical Samples – 100 ng/mL Cutoff

Accuracy of the ONLINE DAT Benzodiazepines Plus assay at a100 ng/mL cutoff was evaluated in method comparison studies between the Benzodiazepines Plus assay and GC/MS results.

Negative Urine Study – One hundred (100) urine samples, obtained from a clinical laboratory where they screened negative in a drug test panel, were evaluated with Benzodiazepines Plus. Ten of these samples were also confirmed negative by GC/MS. Of the 100 samples evaluated, 100 were negative relative to the 100 ng/mL cutoff.

Qualitative Negatives	100	True Negatives	100
Qualitative Positives	0	False Positives	0
Qualitative Total	100		
GC/MS Confirmed Negatives	10		
SemiQuant Negatives	100	True Negatives	100
Semi Quant Positives	0	False Positives	0
SemiQuant Total	100		
SQ Average of True Negs	10.1		
SQ Std Dev of True Negs	13.0		

Positive Urine Study – Eighty-two urine samples were obtained from a clinical laboratory where they were screened positive for benzodiazepines by a commercially available immunoassay. They were subsequently confirmed positive by GC/MS for Oxazepam and/or other benzodiazepines or metabolites (i.e., Lorazepam, Lordiazepam, Nordiazepam, Alprazolam, and Norfludiazepam). Of the 82 samples evaluated, 82 were positive relative to the 100 ng/mL cutoff.

Roche/ Hitachi 917 SemiQuant vs GC/MS GC/MS +	GC/MS -		Roche/ Hitachi 917 Qualitative vs GC/MS GC/MS +	GC/MS -
82	0	+ Test +	82	0
0	10	- Test -	0	10

Acceptance criteria:

Correlation with GC/MS Positives/ Negatives >95%

Accuracy – Clinical Samples – 200 ng/mL Cutoff

Accuracy of the ONLINE DAT Benzodiazepines Plus assay at a 200 ng/mL cutoff was evaluated in method comparison studies between the Benzodiazepines Plus assay and GC/MS results.

Negative Urine Study – One hundred (100) urine samples, obtained from a clinical laboratory where they screened negative in a drug test panel, were evaluated with Benzodiazepines Plus. Ten of these samples were also confirmed negative by GC/MS. Of the 100 samples evaluated, 100 were negative relative to the 200 ng/mL cutoff.

Qualitative Negatives	100	True Negatives	100
Qualitative Positives	0	False Positives	0
Qualitative Total	100		
GC/MS Confirmed Negatives	10		
SemiQuant Negatives	100	True Negatives	100
Semi Quant Positives	0	False Positives	0
SemiQuant Total	100		
SQ Average of True Negs	15.2		
SQ Std Dev of True Negs	16.8		

Positive Urine Study – Seventy-eight urine samples were obtained from a clinical laboratory where they were screened positive for benzodiazepines by a commercially available immunoassay. They were subsequently confirmed positive by GC/MS for Oxazepam and/or other benzodiazepines or metabolites (i.e., Lorazepam, Lordiazepam, Nordiazepam, Alprazolam, and Norfludiazepam). Of the 78 samples evaluated, 76 were positive relative to the 200 ng/mL cutoff. Two results were false negatives by both the semiquantitative and qualitative 200 ng/mL cutoff assays. These results are still within the specifications of 95% agreement with GC/MS reference results.

Roche/ Hitachi 917 SemiQuant vs GC/MS			Roche/ Hitachi 917 Qualitative vs GC/MS	
GC/MS +	GC/MS -		GC/MS +	GC/MS -
76	0	+ Test +	76	0
2	10	- Test -	2	10

Acceptance criteria:

Correlation with GC/MS Positives/ Negatives >95%

Accuracy – Clinical Samples – 300 ng/mL Cutoff

Accuracy of the ONLINE DAT Benzodiazepines Plus assay at a 300 ng/mL cutoff was evaluated in method comparison studies between the Benzodiazepines Plus assay and GC/MS results.

Negative Urine Study – One hundred (100) urine samples, obtained from a clinical laboratory where they screened negative in a drug test panel, were evaluated with Benzodiazepines Plus. Ten of these samples were also confirmed negative by GC/MS. Of the 100 samples evaluated, 100 were negative relative to the 300 ng/mL cutoff.

Qualitative Negatives	100	True Negatives	100
Qualitative Positives	0	False Positives	0
Qualitative Total	100		
GC/MS Confirmed Negatives	10		
SemiQuant Negatives	100	True Negatives	100
Semi Quant Positives	0	False Positives	0
SemiQuant Total	100		

SQ Average of True Negs	18.1
SQ Std Dev of True Negs	17.6

Positive Urine Study – Seventy-two urine samples were obtained from a clinical laboratory where they were screened positive for benzodiazepines by a commercially available immunoassay. They were subsequently confirmed positive by GC/MS for Oxazepam and/or other benzodiazepines or metabolites (i.e., Lorazepam, Lordiazepam, Nordiazepam, Alprazolam, and Norfludiazepam). Of the 72 samples evaluated, 72 were positive relative to the 300 ng/mL cutoff.

Roche/ Hitachi 917 SemiQuant vs GC/MS			Roche/ Hitachi 917 Qualitative vs GC/MS	
GC/MS +	GC/MS -		GC/MS +	GC/MS -
72	0	+ Test +	72	0
0	10	- Test -	0	10

Acceptance criteria:

Correlation with GC/MS Positives/ Negatives >95%

b. Matrix comparison:
Not applicable. The assay is indicated only for urine specimens.

3. Clinical studies:

a. Clinical Sensitivity:
Not applicable. Clinical studies are not typically submitted for this device type.

b. Clinical specificity:
Not applicable. Clinical studies are not typically submitted for this device type.

c. Other clinical supportive data (when a. and b. are not applicable):

4. Clinical cut-off:
Not applicable.

5. Expected values/Reference range:
   Not applicable.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.